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# Somatic genome editing - an overview

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Genome editing has featured frequently in the headlines and is a technology with the potential to revolutionise healthcare. Although a number of genome editing techniques are well established in research, the development of more advanced tools, including the CRISPR system, has brought genome editing into the spotlight.

Genome editing can be performed in germline cells (sperm, eggs or embryos) to induce heritable genetic changes or in somatic cells (other cells) to induce non-heritable changes. Somatic cell editing is much closer to clinical implementation, yet has received far less media attention. In this and related briefings we specifically consider this form of genome editing, the potential clinical impact of this technology, and the ethical and regulatory considerations surrounding current and future use in healthcare.

## Key points

- Modern genome editing techniques provide a relatively flexible and precise means of altering genetic material, offering significant potential for the treatment of several conditions for which there is an unmet clinical need
- Whilst sometimes considered to fit into distinct categories, gene therapies and genome editing technologies could be considered to exist on a spectrum of characteristics and abilities, all affecting the DNA content of the cell in some way
- The ethical concerns raised by the clinical application of genome editing broadly mirror, and in some cases amplify, those raised by more conventional gene therapies
- Genome editing is currently regulated under the existing laws and guidelines governing gene therapies. However, it is likely that in the future regulatory development will be necessary to support appropriate wider clinical uptake

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## What is genome editing?

Genome editing involves the deliberate alteration of a cell's genome through cutting, inserting or otherwise altering DNA. The term is often used interchangeably with 'gene editing'; however, as editing can occur outside genes, 'genome editing' is the more accurate term.

Modern genome editing techniques, in use since the mid-1990s, are not the first technologies capable of altering a genome. Other less precise techniques have been available for decades, primarily as research tools. Naturally occurring phenomena, such as radiation, retroviruses (viruses that insert into host cell DNA) and transposons (mobile genetic elements), have also been used to make alterations to DNA.

### Genome editing and gene therapy

Genome editing is considered by many to be part of the gene therapy toolkit. Gene therapy is a term used to refer to treatments that change the genetic content of a patient's cells to treat disease. Technologies that introduce changes to the genetic content of cells include techniques that do not directly alter the genome, with some simply depositing new genetic material into cells. However, all these technologies raise broadly similar ethical and regulatory considerations.

## Technical features

Some technical features of modern genome editing techniques distinguish them from many other gene therapies; these include:

- **Greater range of changes possible:** Modern genome editing allows for alterations to the genome including the ability to add, delete or alter specified regions of DNA in the target genome. In addition, CRISPR can facilitate the creation of multiple changes at once
- **Increased specificity and genomic integration:** The cutting enzymes of modern genome editing tools can be precisely directed to act on specific regions of DNA, creating high specificity of changes and improved safety compared with undirected integration of DNA into the genome. However, safety concerns around mechanisms for delivery of editing tools remain
- **Increased longevity of effects:** Edits made within the target genome are reproduced as the treated cells divide, whilst sections of DNA that are simply deposited into cells have a limited lifespan
- **Easier production:** These techniques, especially CRISPR, are often easier, cheaper and faster to develop or perform than conventional virus-based gene therapies

These characteristics make genome editing particularly promising for several clinical applications. The potential of modern genome editing to provide a broad range of therapeutic benefits is the foremost ethical justification for its development, but also contributes towards the hype surrounding the technology.

## Ethical concerns

Ethical discussion surrounding human genome editing predominantly focuses on modifying the germline, the impact of such changes on future generations, and the implications of so-called 'designer babies' (the creation of genetically modified embryos). These issues, while important, have diverted attention away from the arguably more pressing issues associated with clinical applications of somatic genome editing.

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There is debate surrounding whether the distinguishing features of modern genome editing create novel ethical considerations over and above those generated by other gene therapy approaches. Some argue that these technologies raise, and perhaps magnify, existing ethical concerns,[1,2] including how to ascertain which conditions are sufficiently 'serious' enough to warrant making genetic changes, distinguishing between medical treatment and human enhancement, and the use of technologies for which the potential adverse effects are not fully understood.

Others suggest that rather than merely incrementally amplifying existing concerns, genome editing technologies pose novel ethical considerations due to the broader context and potential scale of their use. Advances in genome editing techniques have enabled applications that were once considered vague possibilities to become reasonable probabilities.

## Regulatory issues

UK regulation covering gene therapies is drafted broadly, and focuses on the intended purpose rather than the specific technology used. Therefore, somatic cell genome editing is currently regulated under the same framework as existing gene therapies, as an Advanced Therapy Medicinal Product[3]. ATMPs require licensing of clinical trials by the Medicines and Healthcare products Regulatory Agency, and market authorisation from the European Medicines Agency.

The Government[4] (supported by other stakeholders) emphasises that at present there is no need to revise existing legislation. Whilst there seems to be very little clarity about how it might develop, critics argue that regulatory change will be necessary to ensure that existing laws and guidelines are fit for purpose for genome editing applications.

Genome editing utilises different mechanisms to traditional gene therapy, suggesting that different approaches to safety assessment may be required. Revisions might also be needed to clinical trial protocols, to the procedures for patients receiving treatment, and to limit the potential for health tourism. Even in the absence of legislative change, it is likely that regulators will still require more resources for evaluation and oversight as demand increases, costs decrease and the therapeutic potential broadens.

## Policy considerations

Modern genome editing techniques are relatively new, resulting in a limited (though rapidly expanding) evidence base for their use in medicine. Current concerns and considerations surrounding the use of genome editing techniques in a clinical setting include:

- **Biological understanding:** understanding of the human genome has improved rapidly in recent decades, but there is still much to learn about associated processes such as gene regulation and how editing could affect these. However, this concern is not unique to genome editing
- **Uncertainty around off-target effects:** more work is needed to understand the extent to which genome editing techniques cause unintentional secondary edits in the target genome. Progress has been made in increasing precision, though confusion remains and study results in this area are inconsistent
- **Governance:** current frameworks may not be sufficient to deal with an expansion in scope and scale of potential uses of genome editing, and the wider implications surrounding access, resources and social impact

- **Regulation of safety-related issues:** no single standard for somatic genome editing efficiency or specificity can yet be defined. Regulators will need to consider the technical context of the genome editing system in order to account for safety related issues
- **Hype:** genome editing technologies are often reported in 'exceptionalist' terms, leading genome editing to be thought of as distinct from similar techniques. Extensive media coverage has led to speculation about unrealistic uses, and may skew expectations about clinical applications

## Does genome editing warrant special consideration?

Somatic genome editing builds on many of the capabilities of technologies that have existed for some time and is part of the continuum of technological progress of genomic medicine. However, the potential impact of the widespread use of genome editing in medicine on individuals and society may justify special ethical, legal and regulatory consideration aside from other medical technologies.

Two additional policy briefings examine the unique opportunities and challenges arising from clinical application of genome editing and how far the current regulatory landscape may need to evolve in response to technical advances.

## References


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4. Department of Health and Social Care. **Government response to the House of Commons Science and Technology Committee's third report of session 2017-19 'Genomics and Genome editing in the NHS'**. July 2018.



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